Progresses in Biomedical engineering, academic year 2014/2015

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Part 0 - Introduction

Part 1/ Question 1:
What is the mechanism of coincidence detection in post-synaptic membrane of the MSO neuron?
We use analytical description of post-synaptic potential interactions: EPSPs and IPSPs, E+E, E+I, I+E+E, …
MSO processing, inhibition effects/ Laplace transform calculation, comparison to data

Part 2/ Question 2:
How is azimuth encoded (in MSO) in relation to sound frequency?
Sound frequency and simulated time speed changes
Study of just noticeable difference (JND) of ITD using concept of ideal observer, population coding

Part 3/ Question – Task 3:
Look for a technical solution of an ill-posed problem:
Reconstruction of 3D shape of objects from 2D scans. Describe general solution, deliver real-time, real-hardware implementation, write application software…
Aims:
1. Description of the synaptic processing algorithm.
2. Bottlenecks of the ILD computations in the LSO and ITD computations in the MSO.
3. Description of the technical solution.
Introduction to Sound Localization
Introduction to Sound Localization

Stereo sound evokes perception of sound source direction in horizontal plane. What are medial superior olive (MSO) and lateral superior olive (LSO)?

MSO and LSO are nuclei in mammalian auditory brainstem. MSO and LSO contain first binaural neurons. These neurons collect information from both ears (binaural cues).

MSO processes time differences (ITDs) and LSO processes level differences (ILDs).

At low sound frequencies (200 Hz \(\ldots\) < 2 kHz) ITDs are used. At high sound frequencies (1 kHz \(\ldots\) 10 kHz) ILDs are used. Coincidence detection (CD) is the neural mechanism used.

Where in CNS the CD takes place, this is is still debated: \(-\)-delay lines (Jeffress, 1948); \(-\)-cochlear disparity; \(-\)-inhibitory mechanisms; \(-\)-spike correlations
D. Afferent auditory pathway

10 Primary auditory cortex

MGB
Superior Inferior quadrigeminal bodies
Nuc. of lateral lemniscus
Nuc. accessorius
Superior olive
Nuc. cochlearis dorsalis ventralis
Cochlea

Auditory cortex
Medial geniculate body
Inferior colliculus
Nucleus of the lateral lemniscus
Hair cell Dorsal cochlear nucleus
Ventral cochlear nucleus
S-shaped segment Accessory nucleus
Superior olive (olivary complex)
Some binaural neurons of auditory pathway

Model simplifies anatomical connections and enables to test specific sound localization theory

Schematics from [Sanda, Marsalek, 2012]
Horizontal plane sound direction (= azimuth), or binaural hearing (= by both ears, = stereo) uses ITD (= interaural time difference) and ILD (= interaural level difference).

Figure is from [Silbernagl and Despopoulos, 1991, *Color Atlas of Physiology*].
e, elevation, vertical localization;  
α, azimuth, horizontal localization;  
and r, distance of sound source  
(= natural, head centered, spherical coordinates)

- **Elevation**: Ear lobe reflects and amplifies sounds from various directions. ε is detected using (ear lobe and) Head (shape) Related (spectral) Transfer Function, HRTF

- **Azimuth**: is based on a phase difference and intensity difference.

- **Distance**: is also estimated based on the spectral composition of sound. Higher frequencies are damped with distance more than lower frequencies.
Localization in elevation and distance

Head Related (spectral) Transfer Function (HRTF)

Localization in distance: spectral composition, known sounds, movement: Doppler effect

Specific frequency notch suppression changes with elevation
Binaural (= between two ears) distance difference

For azimuth $\alpha$ and head diameter $d$ we get distance difference $D$:

$$D = d_1 + d_2 = d \cdot \sin \alpha$$
What time does it take for sound to travel the distance difference $D$? We call this time ITD, Interaural Time Difference.

$$t = \frac{D}{v}$$

Substitute for the Just Noticeable Difference, $\alpha = 4^\circ$, head diameter $d = 15$ cm, get $D = 1$ cm, use $v = 340$ m/s (sound velocity in the air) and get:

$$t = 30\, \mu s, \text{ (microseconds)}.$$ 

This is paradoxically small for neural detection, because spikes last more than 2 ms.
Outside of the head, branches of hyperbola can be replaced by half-lines.

Outside of the head, rotational hyperboloid is replaced by a cone, sometimes called cone of confusion.

Sound Source

Two ears and the distance between them.

ITD – interaural time delay.

ILD – interaural level difference.

Spectral content – (or HRTF, head shape related transfer function) indicates sound direction in other dimensions.
Steps of Just Noticeable Differences, or Distinguishable azimuths in the frontal horizontal half-plane
Psychophysics
Weber – Fechner law (psycho-physical logarithmic law)

\[ R = 10 \log \left( \frac{S}{S_0} \right) \]

- **R** - (response) subjective intensity
- **S** - (stimulus) physical intensity
- **S_0** – threshold stimulus intensity
- **A** – proportionality constant
Stevens (power) law

\[ R = A(S - S_0)^N \]

- \( R \) - (response) subjective intensity
- \( S \) - (stimulus) physical intensity
- \( S_0 \) – threshold stimulus intensity
- \( A \) – proportionality constant
- \( E \) – constant exponent
Delay lines array theory (by Jeffress)

*a – ipsilateral side branch*

*b – contralateral side branch*

*x – ipsilateral input to the line*

*y – contralateral input to the line*

(ipsilateral = same side
contralateral = other side)

Original delay line array schematics from [Jeffress, 1948]
Critique of Jeffress

• Why this way and not some other way?
• This way means: array of delay lines (example: labeled lines, like in array of olfactory axons for different odors).
• The other way means: one delay does it (example: only few channels, percepts are due to graded responses, like in color vision).
• Decisive point: experimental evidence: array of delay lines was found in birds. The neural circuit wiring in mammals is still unknown.
• Experimental Animals:
  barn owl, (sova pálená, plamienka driemavá, Tyto alba),
  gerbil (pískomil mongolský, Meriones unguiculatus),
  mouse (myš domácí, Mus musculus)
• Experimental Subjects: man (člověk, Homo sapiens).
Delay line theory and other theories

Jefress’ theory proposes delay lines. Inhibitory/stochastic theory proposes few broadly tuned channels. Another theory proposes cochlear delay.
AP responses to ITDs and sound frequencies

Working range of ITD based sound localization are low sound frequencies (here from 100 to 400 Hz). In man this is lower than 1500 Hz. This is set by head size and neural circuit precision.

Model neural circuit with phenomenological spike generation

Figures in Supplementary Information of [Sanda, Marsalek, 2012]
Effect of inhibition

Inhibition subtracts the constant component in the ITD response, widens dynamical range, and shifts phase of maximum away from 0.
Motivation of further work

Spike timing statistics: comparison of acoustic and electric sensation

[Clark, 2008]
Synaptic summation, interaction of excitation and inhibition, coincidence detection and other mechanisms
We have to choose the right PSP form

Common PSP descriptions: alpha function, kinetic model, double exponential and others. We choose: double exponential function.

\[ U = A \left[ \exp \left( \frac{-t}{\tau} \right) - \exp \left( \frac{-t}{\tau_2} \right) \right] H(t) \]

- **Alpha function**

- **Double exponential function**

**Graph parameters:**
- **x-axis:** time
- **y-axis:** normalized voltage
Left: Top: two EPSPs are added (EE)
Bottom: 2 EPSPs and 1 IPSP are added (IEE)

Right: Top and Bottom:
x-axis: ITD (EE delay)
y-axis: maximum voltage (maxU)
Right: x-axis: ITD
y-axis: neuronal firing rates
Curves are symmetrical around the center of the CD window. They are constructed using cumulative distribution functions.

Left: Top: inverse function
y-axis: time window for ITD
x-axis: voltage (threshold value)
Bottom: ditto for the IEE interaction
Model output to pure tones with step 1.414: 50, 71, 100, 141, 200, 283 Hz

Model with phenomenological spike generation, all nuclei from periphery to MSO, arbitrary precision


Same model with detailed auditory periphery according to Meddis, the rest of the circuit up to MSO is the same

[Meddis, papers from 2000 to 2010]
## MSO and LSO working parameters

<table>
<thead>
<tr>
<th></th>
<th>MSO Range</th>
<th>typical values</th>
<th>LSO range</th>
</tr>
</thead>
<tbody>
<tr>
<td>sound frequency [Hz]</td>
<td>70-1400</td>
<td>313/ 4427</td>
<td>1400-14000</td>
</tr>
<tr>
<td>window size [µs]</td>
<td>500-1000</td>
<td>500</td>
<td>7000</td>
</tr>
<tr>
<td>spike timing jitter [ms]</td>
<td>0.125 - 8</td>
<td>1-5</td>
<td>0.125 - 8</td>
</tr>
<tr>
<td>firing rates [AP/s]</td>
<td>out: 20 - 200</td>
<td>60-100</td>
<td>in:100-200 out:&lt;150</td>
</tr>
</tbody>
</table>

## Time warping of typical MSO parameters

<table>
<thead>
<tr>
<th></th>
<th>5 X slower</th>
<th>original values</th>
<th>10X faster</th>
</tr>
</thead>
<tbody>
<tr>
<td>sound frequency [Hz]</td>
<td>28</td>
<td>140</td>
<td>1400</td>
</tr>
<tr>
<td>window size [µs]</td>
<td>3000</td>
<td>600</td>
<td>60</td>
</tr>
<tr>
<td>spike timing jitter [ms]</td>
<td>5</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>(JND) Just noticeable difference [µs]</td>
<td>50</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>detection time by 1 neuron [ms]</td>
<td>3250</td>
<td>650</td>
<td>65</td>
</tr>
</tbody>
</table>
Single neuron JND in dependence on timing jitter

Top:
x-axis: spike timing jitter
y-axis: just noticeable difference (JND) of ITD.
Blue: numerical simulation (arbitrary precision)
Black: exponential fit
Red: estimate with realistic noise, normalized to point (1,1)

Bottom:
Psychoacoustics: minimum audible angle (MAA) in dependence on sound frequency is another name for JND of ITD.
Conclusions:
1. We show analytically tractable description of CD mechanism in post-synaptic membrane of the MSO neuron.
2. Work in progress: description of MSO output sound frequency dependence, exploration of parameter space.

[Grothe, 2003]
Selected Papers and Collaborators


Toth PG, Marsalek P, Synaptic mechanisms of coincidence detection in the sound localization pathway, In preparation.

Thank you for your attention